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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/291,656	PETERS-GOLDEN ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-25 and 27-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-25 and 27-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office Action is in response to the paper filed July 19, 2007.

Claims 1-21 and 26 have been cancelled. Claims 22-25 and 27-37 are currently pending and under examination.

The Board Decision mailed May 30, 2007 has been reviewed. The Board upheld and added additional reasoning as to why the rejection of Claims 22-25 and 27 as being obvious under 35 U.S.C. 103(a) as being unpatentable over Gosselin et al. (USP 5,789,441; priority to February 15, 1996) is maintained. The Board removed this obviousness rejection over Claims 28-37 because they felt that they did not know the limitations of these claims to make the rejection. Thus, the Board rejected Claims 28-37 for being indefinite under 35 USC 112, second paragraph because they considered it unclear as to whether the claims were drawn to a solution or to an article of manufacture for use or sale.

The Board has allowed Applicants to either:

> *(1) Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner ....
>
> OR
>
> (2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record ....

Applicants have chosen to re-open prosecution and have amended Claims 28 and 33 to recite an article of manufacture to define their invention. Additionally, Applicants have amended Claim 22 to recite that the solution consists of, rather than comprises, a vehicle, antibiotic, and leukotrine, and that the vehicle be normal saline.

Maintenance of Rejections:

Claims 22-25 and 27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gosselin et al. (USP 5,789,441; priority to February 15, 1996).

Gosselin et al. teach leukotriene LTB_4 in a sterile liquid (cols. 11-13 and Example I, col. 14, lines 15-16, for example). The term "LTB_4" includes leukotrienes C_4, D_4, and E_4 (col. 6, line 52).

Gossellin et al. do not expressly teach that to include an antibiotic to a solution comprising a sterile liquid and a leukotriene. However, at col. 5, lines 24-29, Gossellin et al. states that the invention provides for the use of an LTB_4 agent as a therapeutic against Gram + and – infections, or fungal infections alone or in association with other antibacterial or antifungal agents.

Therefore, it would have been obvious to a person having ordinary skill in the art to include an antibiotic in a solution comprising a sterile liquid and a leukotriene (Claims 22, 26, 27, 28, 32, 33, 37), wherein the leukotriene is LTB_4 (Claims 23, 29, 34), or wherein the leukotriene is a cysteinyl leukotriene (Claim 24, 3, 35) such as leukotrienes C_4, D_4, and E_4 (Claims 25, 31, 36) because Gosselin et al. suggests to use LTB_4 with an antibacterial or antifungal agent against Gram+ and – infections, or fungal infections.

While the claims recite that the solution aerosolized or is in an endotracheal tube, a bronchoscope, or a nebulizer, for example, these phrases are given no patentable weight. See *Union Oil Co. of California* v. *Atlantic Richfield Co.*, 54 USPQ2d 1227, *In re Rosicky*, 125 USPQ 341; *In re Riden et al.*, 138 USPQ 112; *In re Lerner* 169 USPQ 51. Therefore, the Claims are obvious over Gosselin et al. as set forth above.

Regarding the amendment to Claim 22 that the vehicle be sterile normal saline, it is art-recognized that normal saline is a standard pharmaceutical carrier and that the use of normal saline is a popular/routine choice amongst practitioners in the field in making pharmaceutical compositions.

The Board stated at pages 7 and 8 of their Decision:

Appellants also argue that the '059 Application does not teach "an aerosol" (Br. 7, 10) and that "[b]ecause 'an aerosol' is not functional language the Examiner MUST give this claim element full patentable weight" *(id.* at 8). In particular, Appellants argue that "an aerosol is a composition of matter within its own right" (Reply Br: 3).

While we agree with Appellants that claim 22's "wherein" clause limits the claim to a solution in the form of an aerosol, we do not agree that that limitation distinguishes the claimed solution from that of Gosselin. Appellants define an "aerosol" as a solution in one of two forms: "a gaseous suspension of fine solid or liquid particles" or a "substance... packaged under pressure with a gaseous propellant for release as a spray of fine particles" (Reply Br. 2).

Gosselin does not disclose a solution in the form of a gaseous suspension or under pressure with a gaseous propellant. However, a solution is not changed by the composition of the gas overlying it or the pressure of that gas. A solution comprising a leukotriene, an antibiotic, and a sterile liquid vehicle is the same solution regardless of whether the solution is in an open container (i.e., under air at atmospheric pressure) or whether it is "packaged under pressure with a gaseous propellant." Thus, claim 22's limitation that the "solution is an aerosol" does not distinguish the claimed solution from the solution disclosed by Gosselin and the '059 Application.

We affirm the rejection of claim 22. Claims 23-25 and 27 were not separately argued and fall with claim 22. 37 C.F.R. § 41.37(c)(1)(vii). Since our reasoning differs from that of the Examiner, however, we designate our affirmance as a new ground of rejection under 37 C.F.R. § 41.50(b) in order to give Appellants a fair opportunity to respond.

In the paper filed July 19, 2007, at page 4, Applicants urge that the Examiner and Board have erred in stating that Gosselin et al. provide sterile therapeutic solutions of leukotrienes. The rejection is one of obviousness, not anticipation. The amendment that the vehicle be sterile normal saline does not change the obviousness of the composition. As noted in the rejection, at col. 5, lines 24-29, Gossellin et al. states that the invention provides for the use of an LTB_4 agent as a therapeutic against Gram + and – infections, or fungal infections alone or in association with other antibacterial or antifungal agents. It is art recognized to use saline as a vehicle for

pharmaceutical compositions. Therefore, the amendment does not overcome the teachings of Gosselin et al.

Applicants also urge that the closed nature of Claim 21, that is, changing the claim language from "comprising" to ---- consisting of ---- , is not obvious over Gosselin et al. The phrase is noted, but the Examiner does not consider it to change the obviousness of combining leukotrienes, antibiotics, and saline in a solution. Therefore, the rejection is maintained.

Board initiated Rejection:

Under the provisions of 37 C.F.R. § 41.50(b), we [the Board] enter the following new ground of rejection: Claims 28-37 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite.

As discussed above, claims 28 and 33 are susceptible to two reasonable interpretations. The scope of these claims is therefore unclear. "[A]mbiguity in claim scope is at the heart of the definiteness requirement of 35 U.S.C. § 112, ~ 2." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1342, 65 USPQ2d 1385, 1406 (Fed. Cir. 2003). "A claim is indefinite if, when read in light of the specification, it does not reasonably apprise those skilled in the art of the scope of the invention." *Id.*

In addition, a claim purportedly directed to more than one statutory class of invention is indefinite because it is unclear what would constitute infringement of the claim. Cf Exparte Lyell, 17 USPQ2d 1548, 1551 (Bd. Pat. App. Int. 1990) ("[A] single claim which purports to be both a product or machine and a process is ambiguous and is properly rejected under 35 USC 112, second paragraph, for failing to particularly point out and distinctly claim the invention."); IPXL Holdings, L.L.C. v. Amazon.com, Inc., 430 F.3d 1377, 77 USPQ2d 1140 (Fed. Cir. 2005) (A single

claim covering both an apparatus and a method of using that apparatus is indefinite because it is unclear what acts constitute infringement of the claim).

Here, it is unclear whether claims 28 and 33 are directed to a "solution," as recited in the preamble, or whether infringement would require use or sale of the combination of a solution and a nebulizer or endotracheal tube. We decline to try to harmonize the preamble and "wherein" clauses of claims 28 and 33. If Appellants intend to claim an article of manufacture that comprises a solution and a nebulizer or endotracheal tube, they can amend the claims to clearly recite that: "It is the applicants' burden to precisely define the invention, not the PTO' s. See 35 U.S.C. § 112, paragraph 2 ....[T]his section puts the burden of precise claim drafting squarely on the applicant." In re Morris, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1029 (Fed. Cir. 1997).

If the claims are amended so that they clearly claim an article of manufacture, any rejection would of course need to address the limitation reciting the nebulizer, endotracheal tube, etc. containing the solution.

Claims 29-32 and 34-37 depend on claims 28 and 33, respectively, and are indefinite for the same reason.

Applicants have amended Claims 28 and 33 to recite that they are claiming an article of manufacture as indicated by the Board. It appears that such amendment overcomes the rejection as intended by the Board, but since the Board made the rejection the Examiner will defer to the Board regarding whether the rejection is maintained or not IF this application is ever referred back to the Board for review. For now, the Examiner will hold this rejection in abeyance, allowing the Board discretion at any further prosecution of this application in the future.

Applicants argue that the Examiner has not provided any references sufficient to meet the Boards challenge that she address the article as drawn to the recitation of nebulizer, endotracheal tube, or bronchoscope. The Board stated at page 10 of their Decision:

If the claims are amended so that they clearly claim an article of manufacture, any rejection would of course need to address the limitation reciting the nebulizer, endotracheal tube, etc. containing the solution.

Applicants are urged to review the rejections below.

New Rejection:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide a basis or written description of any article of manufacture comprising a solution of sterile liquid vehicle, an antibiotic, and a leukotriene in an endotracheal tube, bronchoscope, or nebulizer. Throughout the specification, the solution is delivered to the subject via an endotracheal tube, bronchoscope, or nebulizer. The specification does not teach or suggest a manufactured product in which the solution is preloaded into an endotracheal tube, bronchoscope, or nebulizer for use or sale. Therefore, the specification lacks written description of this newly claimed invention, and this amendment is considered to add new matter to the disclosure.

Evidence for the entry of new matter lacking written description in the disclosure is found at the following passages throughout the specification.

Page 3, line 24:

The present invention contemplates the use of leukotrienes and other products of the 5-lipoxygenase pathway as an adjunct in the treatment of pneumonia and other lower respiratory tract infections.

Page 4, line 7:

Importantly, intrapulmonary administration of LTB_4 partially overcame the *in vivo* impairment in bacterial clearance observed in knockout mice.

Page 4, line 14:

The present invention contemplates the treatment of patients with a recognized predisposing factor *(e.g.,* smoking, alcoholism, diabetes, HIV infection, known aspiration) for overwhelming pneumonia, or with early pneumonia, with administration via inhalation or an endotracheal tube of metabolic products of the 5-lipoxygenase pathway *(e.g.,* leukotrienes).

**Note that the endotracheal tube is only being used as a route of adminstration for solution administration but is considered to be an article of manufacture for use or sale.

Page 5, line line 21:

In still further embodiments, the method of administering comprises pulmonary administration, and the pulmonary administration is by aerosolization of the therapeutic composition in other embodiments.

Page 6, line 2:

In still further embodiments, the method of administering comprises pulmonary administration, and the pulmonary administration is by aerosolization of the therapeutic composition in other embodiments.

Page 8, line 23:

For example, a composition for aerosolized pulmonary administration must be formulated such that the product is pharmacologically active following delivery to the lungs.

Page 18, line 27:

Indeed, the present invention contemplates the administration of products of the 5-LO metabolic pathway, particularly LTB_4 and LTC4, independently and as an adjunct *(e.g.,* with antibiotics) to the treatment of pneumonia and other respiratory tract infections caused by a panoply of organisms.

Page 20, para. 1:

Moreover, while the present invention contemplates *in vivo* pulmonary administration of leukotrienes and other 5-LO products to augment defense against bacteria in leukotriene-deficient hosts, the present invention also contemplates *in vivo* administration to patients who are not leukotriene-deficient; indeed, such use is supported by the fact that *in vitro* incubation with exogenous leukotrienes augments phagocytosis and killing by normal macrophages.

Page 21, line 15 through Page 22, para. 2:

...The present invention contemplates using therapeutic compositions of products of the 5-LO metabolic pathway that are indicated as being efficacious based on application of the screen described above. It is not intended that the present invention be limited by the particular nature of the therapeutic preparation. For example, such compositions can be provided together with physiologically tolerable liquid *(e.g.,* saline), gel or carriers or vehicles, diluents, adjuvants and excipients, such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharin, cellulose, magnesium carbonate, and the like, and combinations thereof. These compositions typically contain 1%-95% of active ingredient, preferably 2%-70%. In addition, if desired the compositions may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, stabilizing or pH buffering agents or preservatives. Generally speaking, the nature of the composition will depend on the method of administration.

These therapeutic preparations can be administered to mammals for veterinary use, such as with domestic animals, and clinical use in humans in a manner similar to other therapeutic agents. In general, the dosage required for therapeutic efficacy will vary according to the type of use and mode of administration, as well as the particularized requirements of individual hosts and the organism involved.

A preferred mode of administration comprises administration to the lung. Patients who are sick enough to require mechanical ventilation can receive treatment with pharmacologic agents administered via the endotracheal tube which is connected to the ventilator. Alternatively, intrapulmonary delivery of pharmacologic agents to patients not requiring mechanical ventilation can be accomplished via aerosolization. Alternatively, the agent may be administered to the lung through a bronchoscope. Of course, the therapeutic agents may be investigated for their efficacy via other routes of administration, including parenteral administration. However, when the site of infection is the lung, targeting drug delivery thereto is likely to minimize side effects and systemic consequences.

In the Examples: Page 28, line 25:

In Vivo Administration of Anti-leukotriene Drugs and Leukotrienes

Doses of 5-LO inhibitor (A-79175; Abbott), LTB4 receptor antagonist (CP-105,696; Pfizer), and cysteinyl leukotriene receptor antagonist (MK-571; Merck Research Laboratories) are suspended in methylcellulose and administered once per day orally to unanesthetized mice using a 22 gauge gavage needle.

Page 41, line 2:

LTB4 was administered together with the intratracheal inoculum of K. *pneumoniae* (50 CFU).

Page 41, line 13:

FIG. 10 graphically depicts the effect of intratracheal administration of LTB4 on defective bacterial clearance of the lung in 5-LO knockout mice (each value represents the mean _+ SEM).

Page 51, line 5:

Knockout mice are given 50 CFU of K. *pneumoniae* intratracheally together with LTB_4 in doses ranging from 1-20 ng per animal (6 ng was the dose utilized in the experiment corresponding to FIG. 10); a similar dose range of LTC4 is also tested.

Page 51, line 22:

Once again, knockout mice (n=I 0 animals per group) are inoculated with 50 CFU of *K. pneumoniae* alone or together with optimal doses of LTB4, LTC4, or both leukotrienes; survival is monitored over 14 days.

Page 53, line 1:

The early and late 5-LO metabolite can be selected independent of each other; in other words, LTB4 can be utilized for one dose and LTC4 for the other dose. The second regimen entails continuous administration of leukotriene(s) by aerosol. To ensure dosing limited to the respiratory tract and to be able to precisely quantitate the dose administered, leukotrienes are nebulized and administered to mice via a nose-only exposure chamber.

In no place does the specification teach to make an article of manufacture for use or sale, said article of manufacture comprising a solution of vehicle, antibiotic, and leukotriene placed into an endotracheal tube, bronchoscope, or nebulizer. The specification only teaches the use of endotracheal tubes, bronchoscopes, and nebulizers as routes of administration for the solution, but not as a package or kit for use or sale.

The prior art does not teach preloading endotracheal tubes or bronchoscopes with pharmaceutical composition. By definition, an endotracheal tube is used for airway management and ventilation. See the web at en.wikipedia.org/wiki/Endothracheal_tube. USP 4,821,714 to Smelser, for example, teaches the use of endotracheal tubes as a route for drug administration (see "24" on Figures 4 and 6), but the Examiner finds no examples wherein an endotracheal tube is preloaded with pharmaceutical solutions for use or sale.

Bronchoscopes are viewing devices that allows for the visual examination of lower airways. Brochoscopes are generally used for tissue collection, but can be a route of administration for pharmaceuticals. See the web at answers.com/topic/bronschoscopy?cat=health. The Examiner finds no examples wherein bronchoscope is preloaded with pharmaceutical solutions for use or sale.

Therefore, the specification lacks written description for the newly claimed invention, and finds this invention to be new matter added to the disclosure.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen Cochrane Carlson PhD

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